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FINNEGAN HENDERSON FARABOW
GARRETT AND DUNNER
1300 I STREET NW
WASHINGTON DC 20005-3315

PARKIN, EXAMINER	
ART UNIT	PAPER NUMBER
1813	

DATE MAILED:
07/02/96

Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Office Action Summary	Application No. 08/466,921	Applicant(s) Alizon et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Group Art Unit 1813

☒ Responsive to communication(s) filed on *6/13/96* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *23-31* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment

1. Acknowledgement is hereby made of the Response and Amendment filed March 28, 1996, in which claims 1, 2, 5-7, 9-12, and 15-17 were canceled and new claims 23-29 submitted. A Supplemental Amendment was filed June 13, 1996, introducing new claims 30 and 31.

2. Applicants claimed foreign priority rights under 35 U.S.C. § 119 corresponding to a United Kingdom application, Serial No. 84.23659, filed September 19, 1984. At the time of the previous office action this document was not available for perusal. Applicants expeditious submission of this document is acknowledged.

3. Acknowledgment is hereby made of applicants' amended Abstract.

4. The previous rejection of claims 15-17 under 35 U.S.C. § 112, first paragraph, is hereby withdrawn in response to applicants amendment.

5. The previous rejection of claims 1, 2, 5-7, 9-12, and 15-17 under 35 U.S.C. § 112, second paragraph, is hereby withdrawn in response to applicants amendment.

6. The previous rejection of claims 1, 2, 5-7, and 9-12 under 35 U.S.C. § 102(a) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as being unpatentable over Arya et al. (1984, Science

225:927-930), is hereby withdrawn in response to applicants amendment.

7. The previous rejection of claims 1, 2, 5-7, and 9-12 under 35 U.S.C. § 102(e) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as being unpatentable over Levy (1987, US PAT No. 4,716,102), is hereby withdrawn in response to applicants amendment.

8. The previous rejection of claims 15-17 under 35 U.S.C. § 102(b) as being anticipated by Wain-Hobson et al. (1985, Cell 40:9-17), is hereby withdrawn in response to applicants amendment.

New Grounds of Rejection

9. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the disclosure is not commensurate with the scope of the claims. New claims 23-31 are directed towards DNA restriction fragments, vectors containing said fragments and transformed host

cells. The specification provides a preliminary restriction map of LAV cDNA (e.g. pLAV75, pLAV82 and pLAV13) and lambda phage clones (e.g. λJ19 and λJ81) (refer to Figures 1 and 2). The restriction coordinates are disclosed on page 4, as well as a series of restriction fragments believed to correspond to the *gag*, *pol* and *env* coding regions (e.g. *Pst*I (800 nt)/*Kpn*I (3500 nt); *Kpn*I(3,500 nt)/*Bgl*II (6,500 nt); *Kpn*I (6,100)/*Bgl*II (9150). The specification does not disclose any other HIV/LAV viral clones or restriction fragments *ipsis verbis*.

The instantly claimed invention is directed towards any HIV-1 DNA fragment "having the sequence" disclosed in the approximated restriction fragment. The broadly recited claim language is not supported by the specification. Applicants do not provide any guidance pertaining to the nucleotide sequence of any particular HIV-1 DNA fragment nor do they provide any guidance pertaining to the location of restriction sites from disparate isolates or strains. It is art-recognized that the *Lentivirinae* display considerable genomic heterogeneity and exist as a quasispecies (Holland et al., Curr. Topics Micro. Immunol. 176:1-120, 1992; Goodenow et al., J. Acquir. Immune Defic. Syndr. 2:344-352, 1989). Holland and colleagues concluded (refer to Summary, page 16) that "RNA virus mutation frequencies generally approach maximum tolerable levels, and create complex indeterminate quasispecies populations in infected hosts. This usually favors extreme rates of evolution, although periods of relative stasis or equilibrium, punctuated by rapid change may also

occur (as for other life forms). Because complex quasispecies populations of RNA viruses arise probalistically and differentially in every host, their compositions and exact roles in disease pathogenesis are indeterminate and their directions of evolution, and the nature and timing of "new" virus outbreaks are unpredictable." [Emphasis added by Examiner].

Goodenow and colleagues examined HIV genetic diversity using a novel amplification assay. The authors reported (refer to DISCUSSION, pages 349-351) that:

> RNA viruses have been described as quasispecies (1, 20, 21), i.e., there is no such thing as a viral sequence per se but sets of clusters of closely related sequences. Such is the case for HIV. From any set of data that has been derived, it was simple to calculate that every HIV viral genome within an isolate was unique. This in turn meant that the rate of nucleotide minsincorporation was greater than 1 X 10^{-4}/base/cycle of replication...The potential of the HIV-1 virus to change is thus enormous...In conclusion, we are faced by a virus of enormous complexity, certainly more heterogeneous than influenza A or poliovirus. [Emphasis added by Examiner].

Thus, it seems that any particular restriction fragment will contain a unique nucleotide sequence depending upon the source of the clone. However, the specification does not provide any data concerning the precise nucleotide sequences of the instantly claimed restriction fragments. How would the skilled artisan, who has identified HIV molecular clones from a different source, know if he were in possession of the applicants invention? Absent further guidance from the specificaiton, it would require undue experimentation to practice the invention as presently claimed. Accordingly, claims 23-31 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set

forth in the objection to the specification.

This rejection may be obviated by amending the claim language to recite restriction fragments obtained from specific clones (i.e. An HIV-1 *Bam*HI/*Bgl*II λJ19 cloned DNA restriction fragment wherein said *Bam*HI site is located at nucleotide 8,150 and said *Bgl*II site is located at nucleotide 9,150).

10. Claims 23-31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims contain the recitation "at approximately" in reference to the location of particular restriction sites. This recitation precludes identification of the precise location of said restriction sites. For example, would a *Bam*HI site at 8,000 nucleotides be encompassed by the claim language? Would a site at 8,100 nucleotides be included? Accordingly, the metes and bounds of the patent protection desired can not be ascertained. Applicants may obviate this rejection by reciting the source of the restriction fragment (i.e. clone λJ19) and precise location of the restriction site.

11. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Group 1813 is **(703) 305-7939.** Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

13. Any inquiry concerning this communication should be directed to **Jeffrey S. Parkin, Ph.D.** whose telephone number is **(703) 308-2227.** The examiner can normally be reached Monday through Friday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, **Ms. Christine Nucker** can be reached at **(703) 308-4028.** Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1813

June 23, 1996

ROBERT D. BUDENS
PRIMARY EXAMINER
GROUP 1800